REMARKS

Claim 1 has been amended to obviate the objection to asserted new matter in the term "normal scarring" and to clarify that the method is applied to a subject that has incurred injury or will incur injury at a known surgical site. It will be noted that in both instances, the method is to reduce scar formation as opposed to inhibiting TGF-β1 *per se* and as opposed to inhibiting or preventing scar formation as set forth in former claim 10. Thus, applicants believe that claim 1 is directed to the elected invention and further clarifies the invention as claimed. Claims to non-elected inventions have been canceled. Claims 6 and 7, which were withdrawn, remain since they represent non-elected species which would be rejoined upon allowance of a generic claim.

New claim 23 specifies the location of the wound and is supported in the specification at page 13 line 9 and page 14 lines 5 & 7. New claim 24 simply specifies a portion of claim 1. New claim 25 is supported, for example, on page 15 in paragraph 4 and on page 14 in the third full paragraph. Support for new claim 26 is found on page 15, first paragraph.

No new matter has been added and entry of the amendment is respectfully requested.

It is believed that the amendments address the grounds for rejection by clarification of the invention.

The Invention

As explained in the specification, the present applicants have discovered that by inhibiting the activity of convertase enzymes at a wound site, the amount of active TGFβ at the site is reduced and thus the amount of scarring is also reduced. (See pages 8-9, end of the bridging paragraph.) As noted on page 6, the convertase enzyme furin is involved in the activation of mature latent TGFβ at

the site of the wound and that this activity initially occurs intracellularly in the platelet and then continues as the platelet contents are released on degranulation. Thus, this conversion of TGFβ from its latent to active form by furin convertases occurs locally at the wound site. The claims require, therefore, that the furin inhibitor be administered directly to the wound site. This feature is not disclosed or suggested by Dubois.

The Rejection Under 35 U.S.C. § 102

Claims 1-3 were rejected as assertedly anticipated by Dubois (CA 2,312,109). Respectfully, applicants believe that the interpretation placed upon Dubois by the Office is not correct. Specifically, contrary to the assertion of the Office on page 6 of the Office action, Dubois does not teach applying furin inhibitor to the site of the wound. Applicants are unable to find in Dubois any such disclosure.

The Office is correct that the description of diseases on page 8 in paragraph 2 of Dubois includes "abnormal wound healing" which, as would be implied by its inclusion in paragraph 2, involves addressing this by attacking systemic problems. The paragraph also notes "degenerative cartilage loss following traumatic joint injury" which, however, could not be classified as a "wound." In the discussion of the administration of Dubois' preferred PDX compound, the procedures are quite generic. Among many other possibilities is listed in the first full paragraph on page 12, "implantation" at a desired target site; this is in the context of slow-release compositions. But it is not clear that the target site is a wound. The bridging paragraph on pages 12-13 discusses topical administration among many others but fails to suggest application directly to a wound.

In short, in the five or six pages devoted to techniques for administration starting on page 13 and continuing to page 16 of Dubois, applicants are unable to find any nexus between treatment of abnormal wound healing and any administration directly to the site of the wound.

In view of this failure, Dubois falls short of the legal requirements for a finding of anticipation. In order to anticipate, each and every element of the claimed invention must not only be found in the cited document, the elements must be arranged and connected as described in the claim.

This principle was recently embodied in a District Court decision in *Daiichi Pharmaceutical Co. v. Apotex*, 83 USPQ2d 1471 (DCNJ 2006) where claims were directed to a method of treating otopathy which comprises the topical otic administration of an amount of ofloxacin or a salt thereof effective to treat otopathy in a pharmaceutically acceptable carrier to the area affected with otopathy. The defendants asserted invalidity on the basis of anticipation by two German patents that disclose topical preparations of gyrase inhibitors including ofloxacin. Several other sections of the patent were quoted as including pharmaceutical preparations in dosage units and the disclosure that the invention could be used to treat otitis in dogs and cats. The Court concluded that this was a "piecemeal" interpretation of the German patent and stated that "cherry-picking sections from different pages does not satisfy the burden to show anticipation."

The Daiichi court cited *ATD Corp. v. Lydall, Inc.*, 159 F3d 534, 48 USPQ2d 1321 (Fed. Cir. 1998) for the proposition that an anticipating reference must describe the patented subject matter sufficiently that its existence is recognized by persons of ordinary skill. It also cited the CCPA decision in application of *In re Arkley*, 455 F2d 586, 172 USPQ 524 (CCPA 1972) which overturned a rejection for anticipation of a claim to a single cephalosporin C_a compound over a

disclosure of a genus which included it and also described specific examples of precursors which would lead to the compound of the claim if treated with a particular reagent which was also disclosed in the cited document. The Court overturned the anticipation rejection on the grounds that the reference did not clearly and unequivocally disclose the claimed compound or direct those skilled in the art to the compound without any need for picking, choosing and combining various disclosures not directly related to each other by the teaching of the reference.

Similarly, here, there is insufficient specificity in the teachings of Dubois to lead the reader to understand that in order to reduce scarring, a furin inhibitor should be applied directly to the wound. Accordingly, this basis for rejection may properly be withdrawn.

The Rejection Under 35 U.S.C. § 103

Claims 4 and 5 were rejected as assertedly obvious over Dubois in further view of Pearton (*Exp. Dermatol.* (2001) 10:193-203). This basis for rejection assumes that Dubois teaches the invention as claimed in claims 1-3, which has been demonstrated not to be the case above. Thus, the rejection for obviousness fails for this reason alone.

However, it fails for an additional reason. There is no teaching or suggestion in either Pearton or Dubois that the furin inhibitor must be one that inhibits the formation of active TGFβ at the site of wound healing. It may be true that the PDX compound described in Dubois does inhibit TGFβ activation, however, such an intrinsic or inherent property cannot provide a suggestion necessary to support a rejection based on obviousness. Thus, this basis for rejection fails in view of the additional limitation of claim 1 that the furin inhibitor inhibits TGFβ activation. Neither document suggests this property which is the basis for applicants' invention. Accordingly, this basis for rejection may also be withdrawn.

The Rejection Under 35 U.S.C. § 112, Paragraph 1 – Written Description

Applicants appreciate the withdrawal of the previous rejection based on lack of enablement.

Claims 1-5 are said to be rejected under this provision, although applicants believe claim 5 is included in error in light of the reasoning set forth therein. The basis for this rejection appears to be that there is insufficient structural definition of the compounds included within the invention.

However, in view of the wide variety of furin inhibitors that are known in the art and in view of the description in the application which permits the ordinary practitioner to test which of these have the desired property of inhibiting TGFβ activation, applicants respectfully submit that the written description requirement is met. For example, furin inhibitors are disclosed in:

Lu, W., *et al., J. Biol. Chem.* (1993) 268:14583-14585;
Jean, F., *et al., Biochem. J.* (1995) 307:689-695;
Dahlen, J. R., *et al., J. Biol. Chem.* (1998) 273:1851-1854; and
Basak, A., *et al., Biochem. J.* (1999) 338:107-113.

Copies of these documents are enclosed for the convenience of the Office.

Thus, there was a plethora of candidate furin inhibitors available in the art at the time the invention was made.

The application describes, on page 24, a method for assessing the formation of active TGFβ in platelets using the PAI luciferin bioassay described by Abe, *et al., Anal. Biochem.* (1994) 216:276-284. In this assay, TGFβ causes expression of luciferase in genetically modified mink lung epithelial cells, which then cleaves luciferin to provide a luminescent reaction. Thus, one need only supply the art-known furin inhibitor candidate to the compositions subjected to this assay as described on page 24 in order to confirm the ability to activate TGFβ.

Since the structures of furin inhibitors are known in the art, and since the application provides a straightforward assay to ascertain which of these inhibitors exhibits the functional limitations set forth in the claim, applicants respectfully submit that the written description requirement is met.

Conclusion

The claims have been amended to clarify that a furin inhibitor that inhibits TGFβ activation is applied directly to the site of a wound where the wound, is the result of an injury incurred by an individual or which will occur at a known location due to expected surgery. Since Dubois fails to disclose this confluence of factors, Dubois cannot anticipate the invention as claimed in claims 1-3, nor does it provide a basis for finding obviousness in combination with Pearton of claims 4 and 5.

Applicants have also demonstrated that the written description requirement is met since furin inhibitors are well known and the application itself describes a method to assure that the required functional characteristic is present. Accordingly, it is believed that the examined claims 1-5 are in a position for allowance, as are new claims dependent thereon, claims 23-26. Applicants believe claims 6-7 may therefore be rejoined and passage of claims 1-7 and 23-26 to issue is respectfully requested.

If minor issues remain that could be resolved by phone, a telephone call to the undersigned is respectfully requested.

In the unlikely event that the transmittal letter is separated from this document and the Patent Office determines that an extension and/or other relief is required, applicants petition for any required relief including extensions of time and authorize the Commissioner to charge the cost of

such petitions and/or other fees due in connection with the filing of this document to **Deposit Account No. 03-1952** referencing docket No. 255352001800.

Respectfully submitted,

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